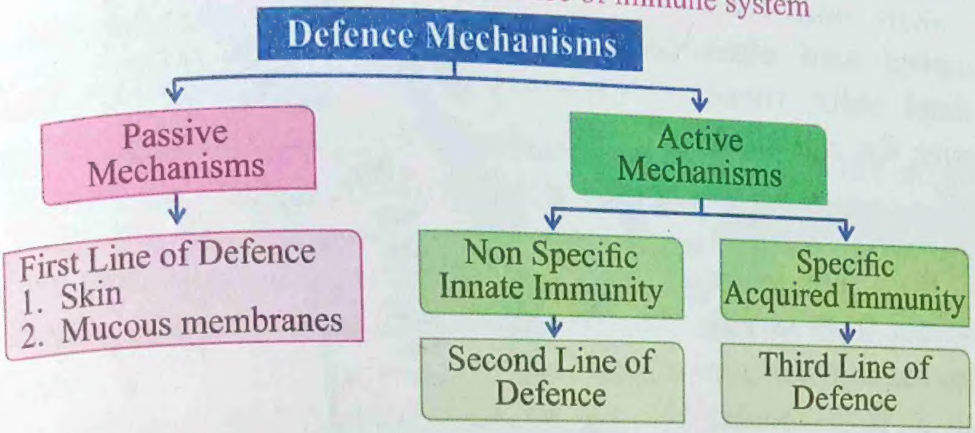
Introduction

We are living in the sea of micro-organisms. Most of these organisms are our friends. However, some of them are our enemies. These enemies invade our body continuously. To counter attack these invaders, our body has developed a system called **immune system.** The immune system consists of many biological structures and processes within an organism that protects against diseases. This ability of an organism to combat diseases and pathogen is called **immunity.** The study of immunity is called **immunology.** In this chapter we will discuss three lines of defence of immune system.

Table 13.1 Lines of defence of immune system



13.1 First Line of Defence (Layered Defence)

The first line of defence is non specific and part of innate immunity (present naturally at the time of birth). It is the best defence as it keeps pathogens out of the body. It consists of following parts.

13.1.1 Skin

Skin is the largest organ of the vertebrate body accounting for 15% of an adult human's total weight. The skin not only defends the body by providing nearly impermeable barrier but also reinforces this defence through chemical weapons on the surface.

Tit bits

The word skin is derived from Latin word "cutis" In mammals it is the largest organ of the body. It has many functions like protection, sensation, heat regulation, control of evaporation, excretion etc.

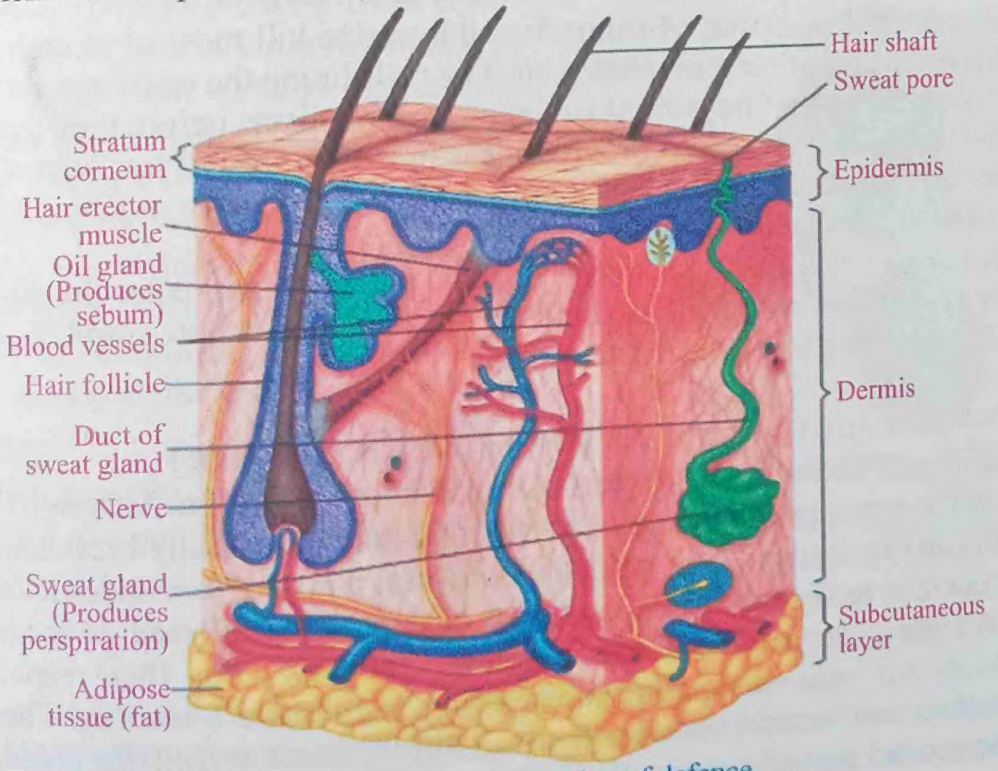


Fig. 13.1 Skin as first line of defence

The skin contains **keratinocytes** and also possesses dead cells, these become barrier for microbes to get entrance.

The dermis of skin produces oil from **sebaceous** glands and sweat from **sweat glands,** gives the skin surface a pH of 3 to 5. It is acidic enough to inhibit the growth of many micro-organisms. Sweat also contains the **lysozymes,** which digest bacterial cell wall. These also contain natural antibiotic (such as lactic acid).

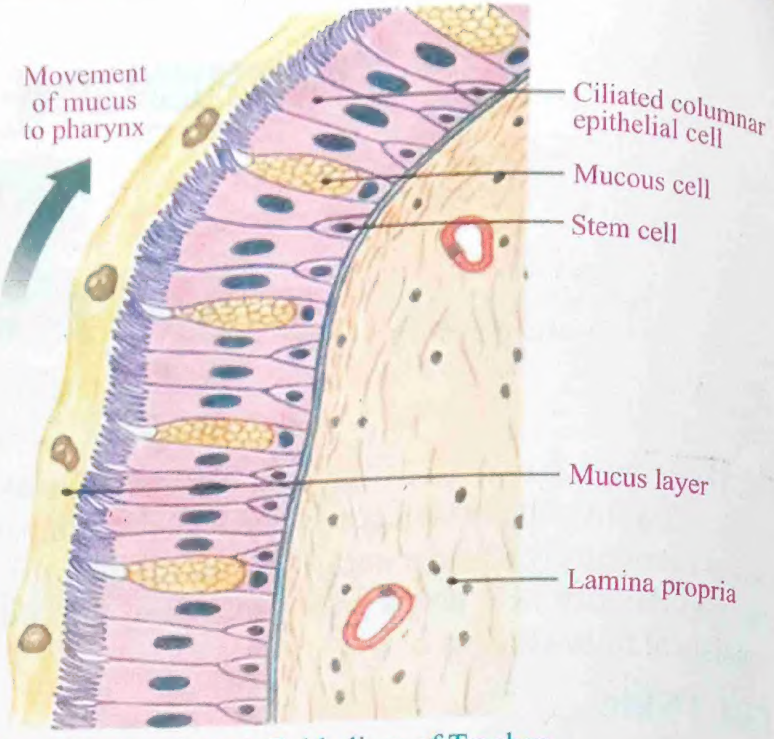


Fig. 13.2 Respiratory Epithelium of Trachea

13.1.2 Digestive and Respiratory tract

Both the digestive and respiratory tract open to the out side and their inner surfaces must also be protected by foreign invaders. Microbes are present in food but many are killed by saliva which also contains lysozyme and $NaHCO_3$. The very low pH of stomach due to HCl, enzymes of stomach and intestine kill most of microbes of food. Micro-organisms also present in inhaled air. The cells lining the respiratory tract secrete layer of sticky mucus that traps most of the micro-organisms before they can reach the warm moist lungs, which would provide ideal breeding ground for them. Other cells lining in these passages have **cilia** that continuously sweep the mucus towards the glottis. There it can be either swallowed or spit out.

Occasionally an infectious agent, called a pathogen will enter the digestive and respiratory system and body will use defence mechanisms such as vomiting, diarrhoea, coughing and sneezing to expel the pathogens.

13.2 Second Line of Defence: (non specific defence)

This line of defence is also a part of innate immune system. Although the surface defences of the vertebrate body are very effective but occasionally breached allowing invaders to enter the body. At this point the body uses a host of non-specific cellular and chemical devices to defend itself. This type of defence is referred as second line of defence. All these devices have one common property i.e., they respond to any microbial infection without pausing to determine the invader's identity. The cells and chemicals of second line of defence, defend the body to attack and kill the invaders.

The second line of defence consists of three types of mechanisms i.e., natural

killer cells, inflammatory responses and temperature responses.

13.2.1 Killing cells of blood

Perhaps the most important of vertebrate body's non-specific defence are the white blood cells called leucocytes. These cells circulate through the body and attack invading microbes within tissue. There are three basic kinds of these cells and each kill invading micro-organism differently.

Do you know?

How neutrophil is different from lymphocytes, second line of defence and third line of defence.

Macrophages :

The macrophages (Big eaters) are large irregularly shaped cells that kill microbes by ingesting them through phagocytosis (like *Amoeba).*

They are found in organs such as lungs, liver, spleen, kidney and lymph nodes rather than remaining in the blood.

They leave the bone marrow and travel into the blood as monocytes, where they develop into macrophages. Once they leave the blood and settle in the organs, they remove any foreign matter found there.

The macrophages are long-lived cells. They play a crucial role in initiating immune response. They do not destroy pathogens completely but cut them up to display antigens that can be recognized by lymphocytes. Macrophages secrete some types of proteins which trigger maturation of monocytes. A protein interleukin-I stimulate the hypothalamus to raise body temperature, and other protein stimulate the specific response.

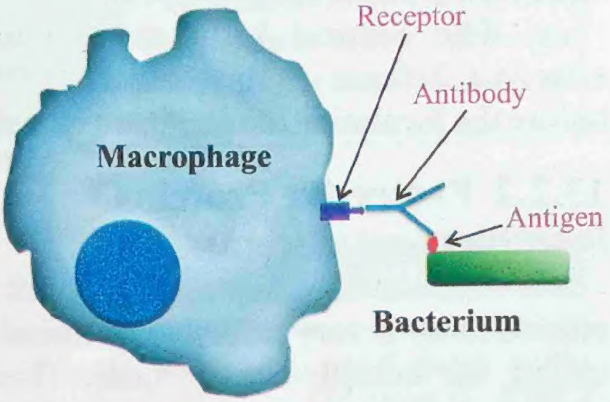


Fig. 13.3 Macrophage

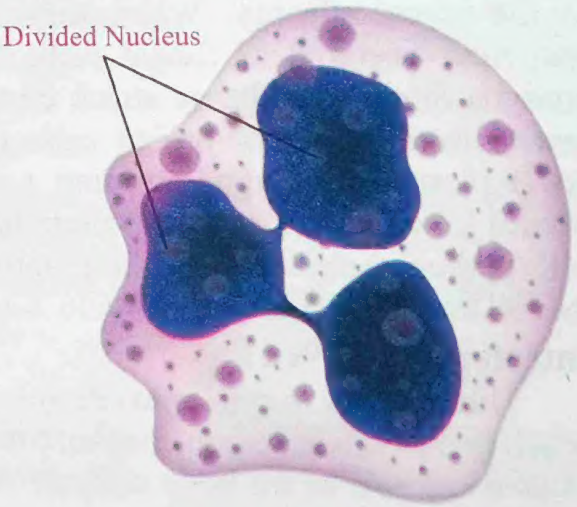


Fig. 13.4 Neutrophils

Neutrophils:

The neutrophils are types of white blood cells that, like macrophages destroy the pathogens by phagocytosis. In addition neutrophils release lysozyme, chemicals that kill other bacteria in the neighbourhood. Neutrophils have short life span, after killing and digesting some pathogens they die. Dead neutrophils are collected at the site of infection to form pus. Due to psuedopodial movement, their body squeeze and can enter all those parts of tissues where other WBC can not enter. These are most abundant types of WBCs in most mammals, about 40 to 70%.

Natural killer cells:

These cells do not attach invading microbes directly instead they kill cells of the body that have been infected. They do not phagocytose microbes but rather by creating a hole in the plasma membrane of target cell. Proteins called **perforins** are released from the membrane of the natural killer cells and inserted into membrane of target cell which then swell and bursts,by a protease (enzyme).

The natural killer cells cause very effective defence against cancer cells usually before the formation of malignant tumor.

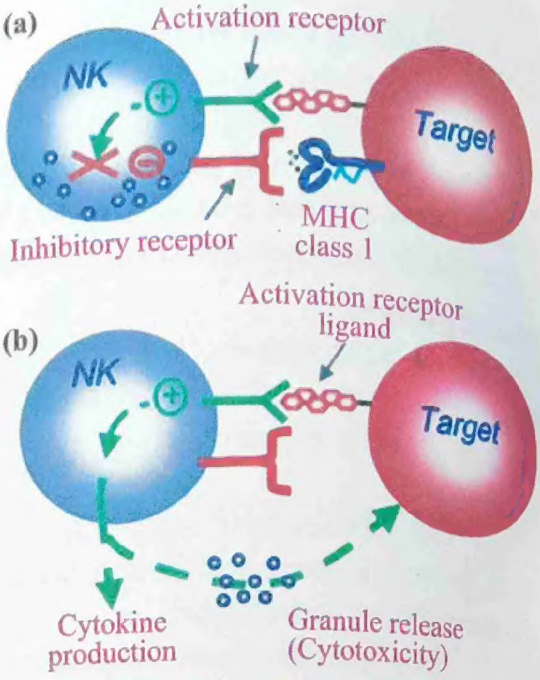


Fig. 13.5 Natural Killer Cell (NK)

13.2.2 Protective Proteins (complement system)

The cellular defence of vertebrates are enhanced by a very effective chemical defence called the complement system. This system consists of approximately 20 to 30 different proteins formed in the liver, that circulate freely in the blood plasma. When these proteins encounter bacterial or fungal cells then these proteins form a membrane attack complex that inserts itself into the foreign cells (pathogen cells) plasma membrane forming a pore like natural killer cells. The water enters the foreign cell (pathogen cells) through this pore causing, the cell to swell and burst.

Interferons (IFNs):

These belong to cytokines (Protein in lymph cells). Interferons is another class of proteins that plays a key role in the body defence. There are three major categories of interferons. These are grouped into two types. Type I, alpha and beta while type II is gamma. These cells of the body synthesize alpha and beta interferons. These polypeptides act as messengers, that protect normal cells in the vicinity of infected cells from becoming infected. Though viruses are still able to penetrate the neighbouring cells. The **alpha and beta interferons** prevent viral replication and protein assembly in these cells. (Thus named interferons means interfere with viral replication inside body cell).

Activity

Justify why the physicians prescribe antipyretic drugs, when fever is a nonspecific defence against microbial infection.

Tit bits

Aspirin reduce the degree of fever because aspirin impedes the formation of prostagladin from arachidonic acid. Drugs like aspirin that reduce fever are called antipyretic.

Activity

How antihistamine therapy is helpful to the patients of runny nose and skin rashes?

Gamma interferon is produced only by particular lymphocytes and natural killer cells. Gamma interferons defend against infection and cancer. These also activate other immune cells such as macrophages and natural killer cells.

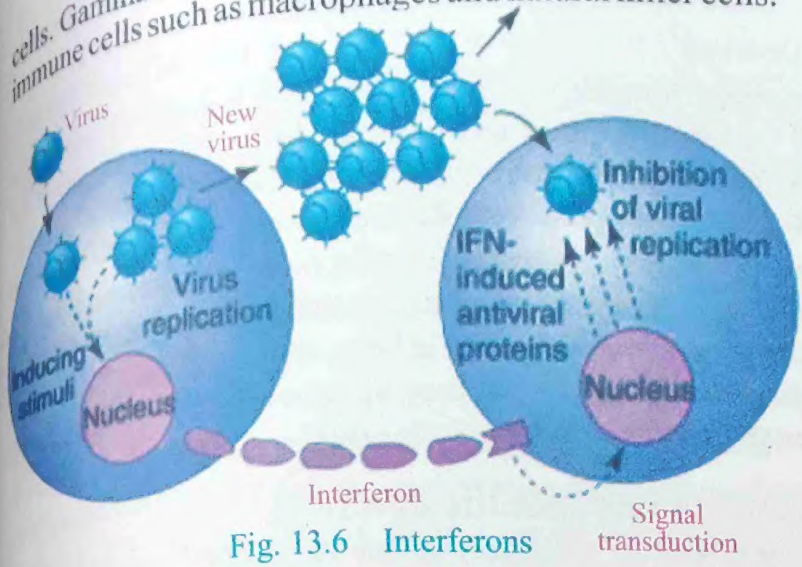


Fig. 13.6 Interferons

Tit bits

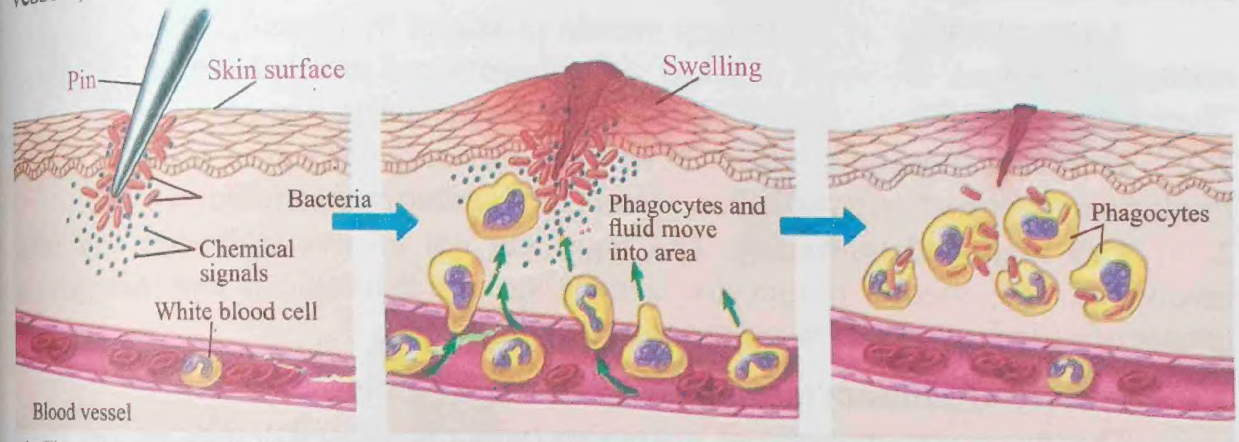
Invading bacteria and viruses are recognized as foreign because they contain molecules, which are different from any of our own molecule. These foreign molecules are known as antigens.

Inflammatory Responses:(means setting on fire)

The inflammatory response is a localized, nonspecific against infection. Infected or injured cells release chemical alarm signals, most notably **histamine and prostaglandins** (Produced from all nucleated cells). These chemicals promote the dilation of local blood vessels, which

Tit bits

Histamine secreted from basophils and mast cells which are a class of WBC. These cells are filled basophil granules found in number of tissues.



1- Tissue injury; release of chemical signals such as histamine

2- Dilation and increased leakiness of local blood vessels; migration of phagocytes to the area

3- Phagocytes (macrophages and neutrophils) consume bacteria and cell debris; tissue heals

Fig. 13.7 Inflammatory Responses

increase the flow of blood at the site of infection or injury and causes the area to become warm, red, swollen and feel pain. They also increase the permeability of capillaries in the area producing **edema.** Phagocytes migrate from the

Activity

Search net to see the difference between two sub classes of monocytes.

blood to the extra cellular fluid where they can attack bacteria. The function of inflammation is to remove necrotic cells and to start rapair process and prevent spreading of infection.

13.2.4 Temperature Responses

Macrophages that encounter invading microbes release a regulatory molecule called interleukin-1 which is carried by blood to the brain. **Interleukin-1** and other **pyrogens** (Greek Pyr=fire) such as bacterial endotoxins cause neurons in the hypothalamus to raise the body temperature several degrees above the normal value of 37°C (98.6°F). The elevated temperature thus results is called fever. Fever contributes to the body's defence by stimulating phagocytosis and causing the liver and spleen to store iron, reducing blood level of iron which bacteria need in large amount to grow. However very high fever is harmful because excessive heat may denature critical enzymes and proteins of body. Therefore, the patient is given antipyretic drugs.

13.3 Third Line of Defence: (The specific defence)

Many of us contract some sort of infection in our child hood, small pox for example, is an illness that many of us experience before we reach our teens. It is a disease of childhood as most of us contract it in childhood stage and never catch it again. Once you have had the disease, you are usually immune to it. The specific immune defence mechanism provides such immunity.

An antigen is a molecule capable of inducing an immune response in the host. These are usually foreign bodies but sometimes these are part of host itself in an autoimmune disease.

An antibody is a "Y" shaped protein produced by plasma cells to destroy or neutralize antigens. These are attached on pathogens and secreted by B. lymphocytes. The third line of defence is specific and most effective consists of two types.

1. **Humoral immunity,** mediated by macromolecules found in the extra cellular fluids such as antibodies, complement proteins and certain antimicrobial peptides.
2. **Cell mediated immunity:** This type does not involve antibodies; but rather involve the activation of phagocytes, antigen specific cytotoxic T- Lymphocytes and release of various cytokines in response to antigens.

13.3.1 Role of Monocytes in Third Line of Defence

The monocytes are types of leukocytes (white blood cells), they are the largest type of leukocytes. As part of vertebrate innate immune system (discussed in second line of defence), monocytes also influence the process of adaptive immunity. There are at least two sub classes of monocytes in human blood.

I) **Dendritic cells:-** These are antigen presenting cells, mark out foreign bodies to be destroyed by lymphocytes.

ii) **Macrophage:-** These are large phagocytic cells.

13.3.2 Role of T-Cells in Third Line of Defence: (cell mediated immunity)

T-Cells or T. Lymphocytes are a type of lymphocytes (a type of WBC) that play a central role in cell mediated immunity. T-cell can be distinguished from other lymphocytes such as B-Cells and natural killer cells by the presence of a T-Cell receptor on the cell surface. They are called T-Cells because they mature in the **thymus** from thymocytes, an endocrine gland in chest (some are synthesized in tonsils also).

Activation of T-Cells: When infection occurs the T-cells detect particular antigen of invading micro-organism by engulfing it. The T-Cells display these antigen on their surface with the help of their own protein known as **Major Histocompatibility Complex** (MHC). In this way, macrophages become **antigen presenting cells (APCs)**. At the same time macrophages release **interleukin 1** that stimulates helper T-Cells and attracts them towards displayed antigen. The helper T-Cells have receptor by which they bind with specific antigen present on APC. The receptor on surface of T-Cells are called T-cell receptor (TCR). The T-cell also stimulated by interleukin to secrete another protein called **interleukin 2** which

> **Tit bits**
>
> *The primary response is slow because at this stage there are very few B-cells that are specific to antigen.*

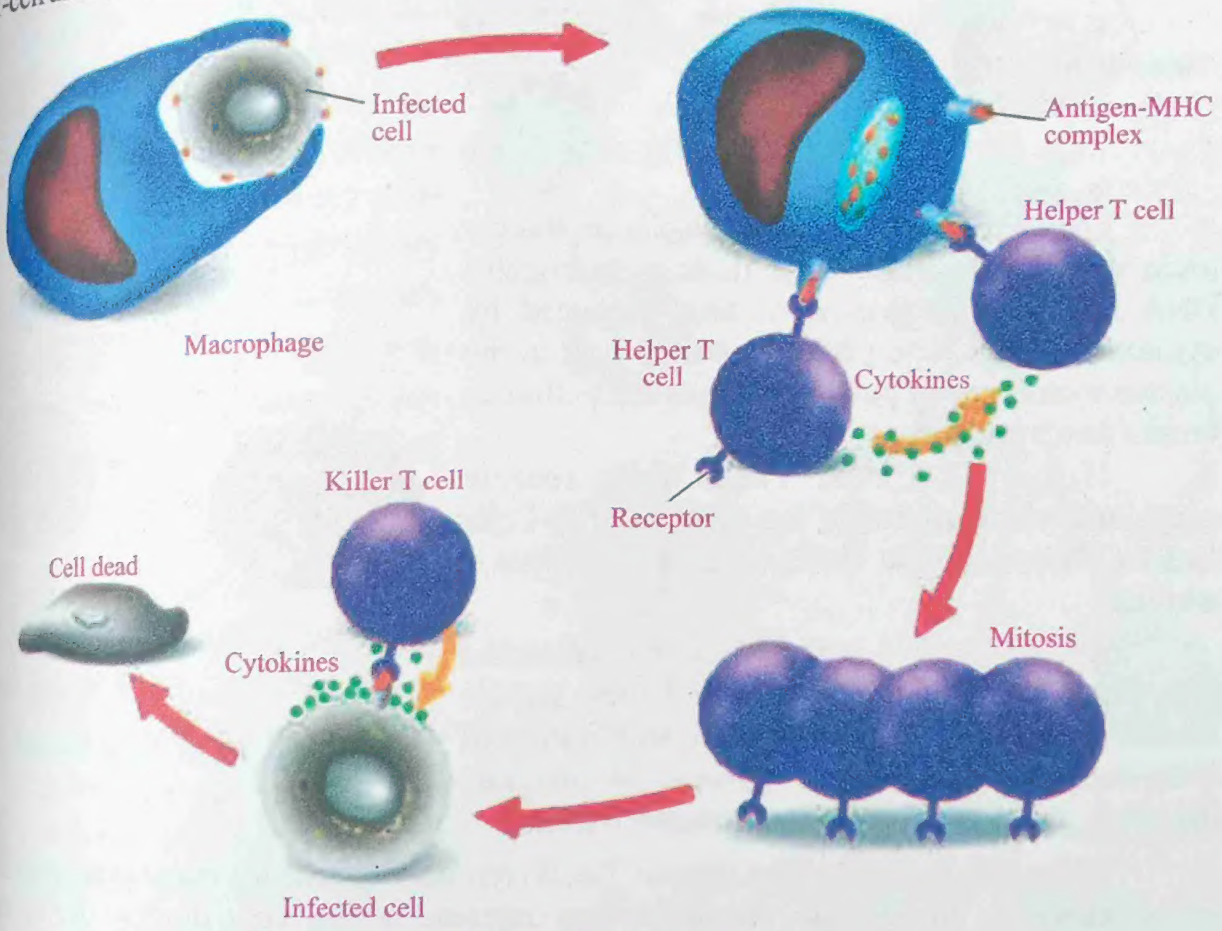


Fig. 13.8 Cell Mediated Immune Response

is not only responsible for division of helper cells but also proliferates certain cytotoxic T- cells and B cells. There are millions of different T-cells, as each type of T-cells respond to a specific type of antigen. This type of immunity is called cell mediated immunity.

Types of T-Cells: The T-lymphocytes are of two types i.e., **CD8** (cluster of differentiation) as they have surface marker CD8, include cytotoxic T-cells and suppressor T-Cells. The other group is helper T-Cells also called **CD4** cells due to presence of surface marker CD4. On activation, the T-Cells divide and produce 4 types of cells, these four types of cell play vital role in cell mediated immune response. The four types of cells produced by T-cells are as follow.

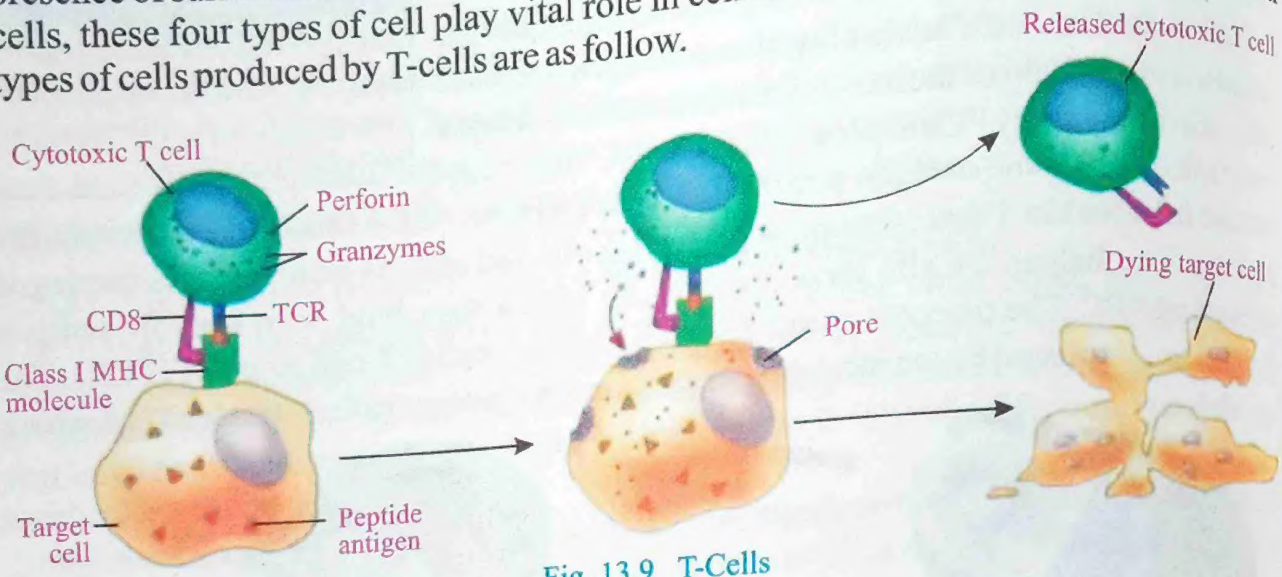


Fig. 13.9 T-Cells

a. Cytotoxic T-Cells: These cells produce a toxin called **cytotoxin.** This destroy pathogen's DNA and perforin protein is also produced by cytotoxic T-cells. The perforin creates hole in the plasma membrane of pathogen as a result pathogen breaks down into pieces.

b. Helper T-Cells: These cells secrete cytokines which stimulate the division of B-Cells and T-Cells to increase defense against pathogenic attacks.

c. Suppressor T-cells: After the successful removal of infection the suppressor T-Cells secrete certain proteins that inhibit further proliferation of T-Cells, Thus immune response is blocked therefore, the cells are called suppressor T-Cells.

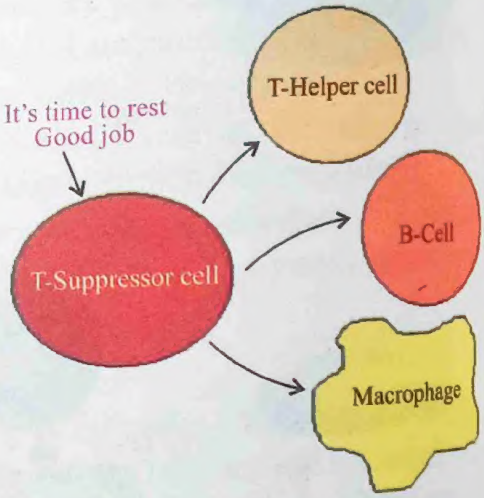


Fig. 13.10 Binary Fission

d. Memory T-Cells: This type of T-cells remain inactive for many years after the initial exposure to antigen. However they become active very quickly during the secondary response to antigen and fight against pathogen.

13.3.3 Role of B-Cells in Third Line of Defence "Humoral immunity" or Antibody Mediated immune response.

The antibodies are small glycoprotein molecules.

B-lymphocytes secrete antibodies, which destroy bacterial pathogens. B-lymphocytes are so called because they develop in the bone marrow and first discovered in the bursa of intestines of birds.

As mentioned earlier in this chapter that antigens are foreign molecules because they are different from any of our own molecules. We have a huge number of B-lymphocytes in our blood each one of them recognizes and responds to one particular antigen. The B-lymphocytes respond by producing antibodies.

Activation of B-Lymphocytes

Most B lymphocytes will spend all their lives without anything happening to them at all because they never meet their particular antigen. But a B-lymplcyte does encounter an antigen which binds to the receptors on its cell surface membrane, it is triggered into action. After encountering its specific antigen, the B-lymphoeyte is stimulated to divide repeatedly by mitosis. Some of these cells differentiate into **plasma cells.** These cells have the ability to produce very large number of antibody molecule in very less time (2000 antibody molecules per second). These antibodies bind with antigens and destroy them.

Other cells produced as a result of mitosis do not secrete antibody, instead they remain as **memory cells**. These cells live for long time and remain circulating in the blood, they are capable of responding very quickly if the same type of antigen enters the body again.

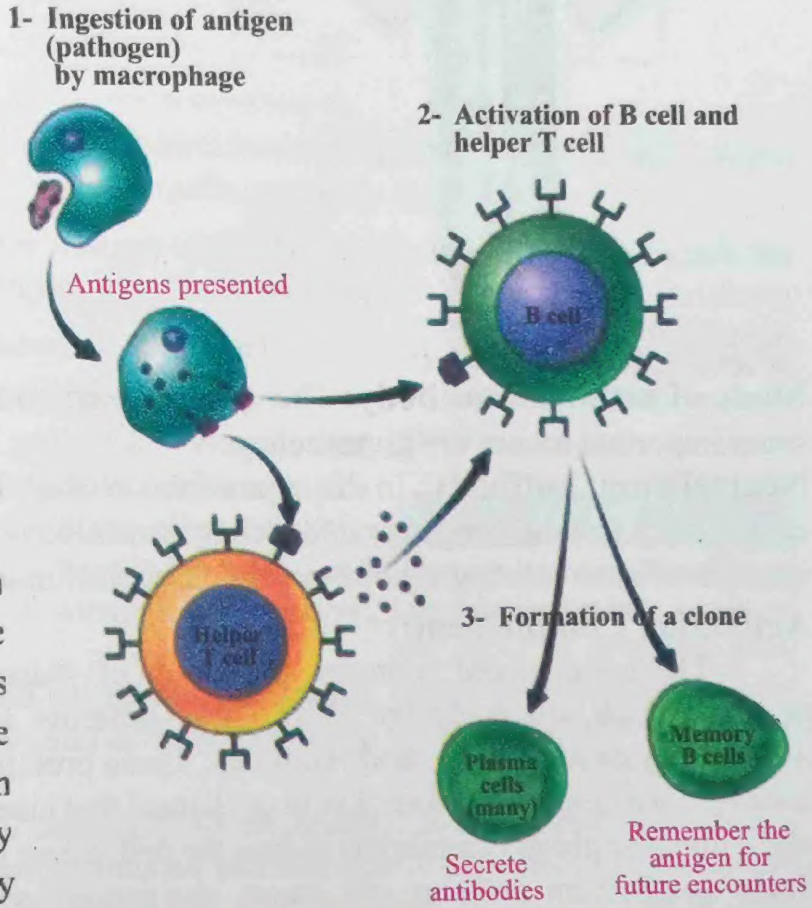


Fig. 13.11 Antibody mediated response

Structure of Antibody:

Antibodies are all globular glycoproteins and form the group of plasma proteins called **immunoglobulins.**

The basic molecule common to all antibodies consisting of four polypeptides chains two **long (heavy) chains** and two **short (light) chains. Disulphide bridge,** hold the chains together. Each molecule has two identical antigen binding sites which are formed by both heavy and light chains. The sequence of amino acids in these regions make the specific three dimensional shape which binds to just one type of antigen. This is the variable region which is different on each type of antibody molecule produced. The hinge region gives the flexibility for the antibody molecule to bind around the antigen.

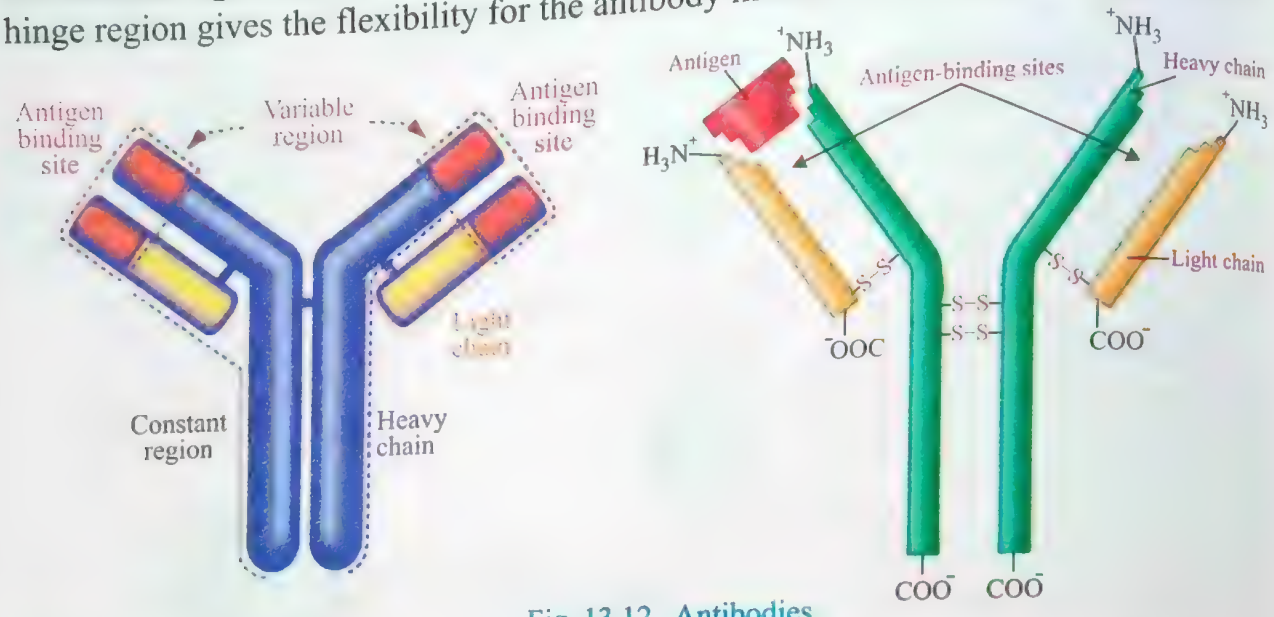


Fig. 13.12 Antibodies

Mode of action of antibody: There are different modes of action of antibodies, some important modes are given below.

Neutralizing antibody: In this type of mode of action of antibody, an antibody that defend a cell from an antigen or infection by neutralizing any effect it has biologically. An example of a neutralizing antibody in diphtheria antitoxin.

Activation Complement:

The complement proteins are group of plasma protein, which are made by liver. These proteins are activated by an antigen antibody complex. These proteins usually cluster together to form a pore or channel that insert into a microbe plasma membrane to lyse the cell. Some of these complement proteins can cause chemotaxis and inflammation. Due to these activities number of white blood cells increase at the site of infection.

Do you know?

There are 5 classes of antibodies i.e. immunoglobulin IgG, IgM, IgD, IgA and IgE.

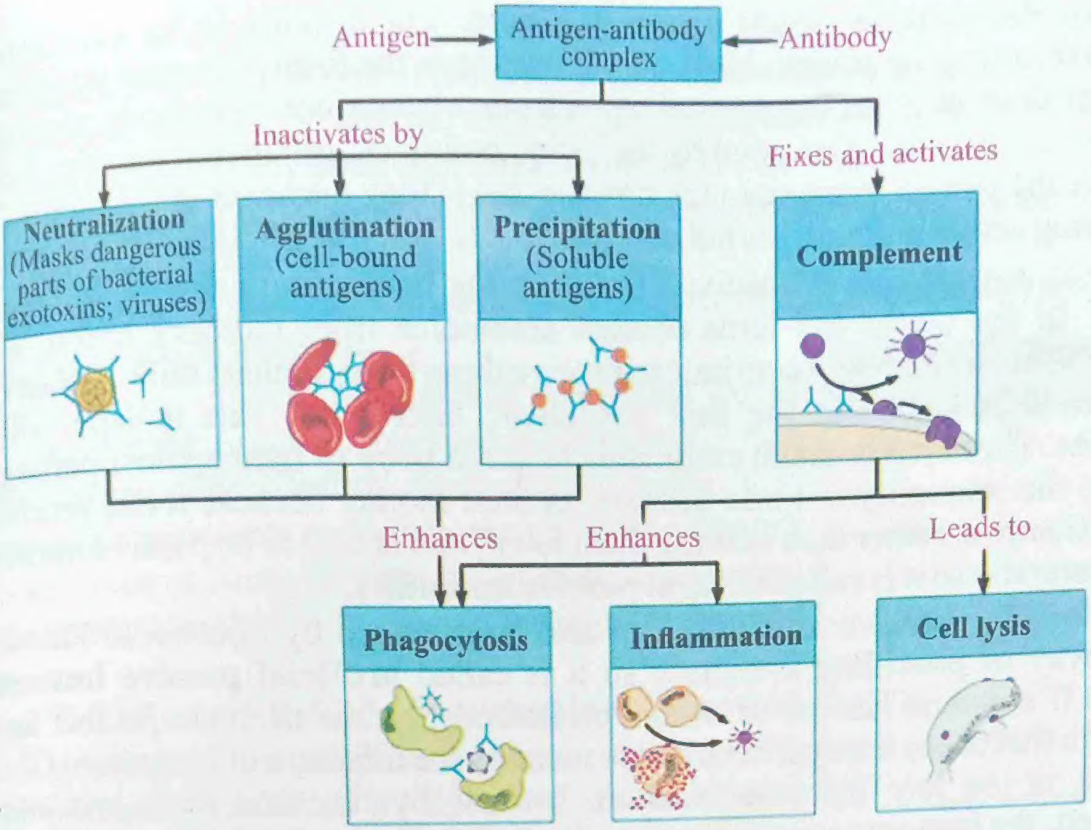


Fig. 13.13 Mode of action of antibody

Precipitating antigens: When antibodies bind to some free antigen, cause the antigen to precipitate out of solution, thus phagocytic cells can easily ingest them.

Facilitating phagocytosis: When antigen antibody complex is formed it signals the phagocytic cells to attack. This complex binds to the surface of macrophages, it facilitates phagocytosis.

Activity

Do you know what are auto grafts ?

13.3.4 Inborn and Acquired Immunity

As discussed in the early part of this chapter that inborn (innate) immunity is non specific and makes the first and second line of defence. On the other hand the acquired (adaptive) immunity is highly specific and develops in reaction of antigens. However, it takes several days to become fully functional.

Tit bits

Organ transplant is a medical procedure in which an organ is removed from donor body and placed in the body of recipient to replace a damaged or missing organ.

Types of acquired or Induced immunity: Acquired immunity may be active or passive and either type may be acquired naturally or artificially.

Active immunity: It is a kind of immunity which develops after contracting pathogen inside the body. The body has been stimulated to make a particular type of antibody and can produce these same ones more quickly in large quantity, if it is exposed to same pathogen again. The immunity has developed naturally, is called as **natural active immunity.**

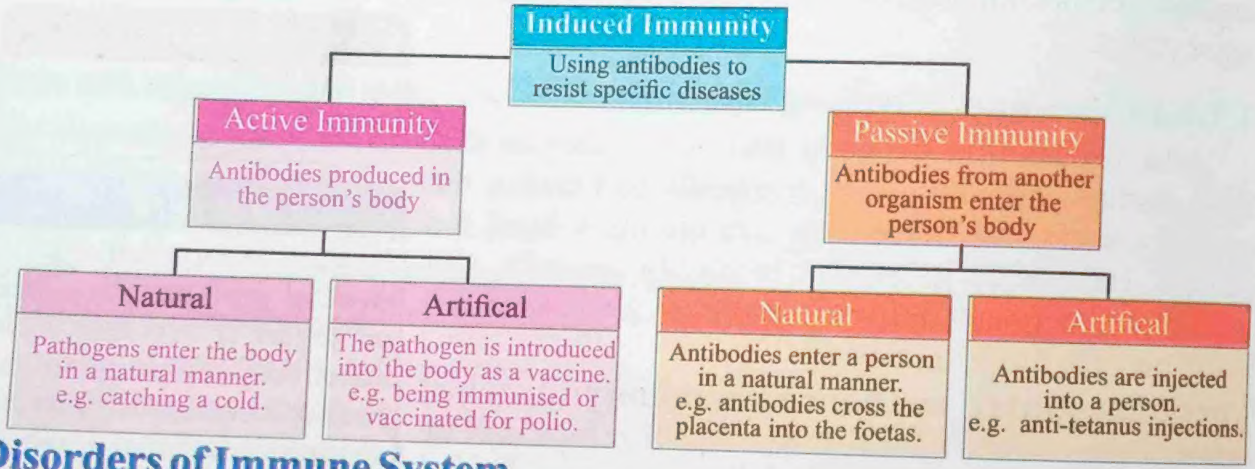
Another way in which active immunity can develop is by vaccination. This involves injecting the antigen into body. It may be in the form of viruses which have been made harmless, or as an inactivated toxin from a bacterium. The body responds in the same way as it would, if invaded by the living pathogen, producing memory cells which will make the person immune to the disease that is they may ever encounter it. This way of acquiring active immunity is not natural. So it is called **artificial active immunity.**

Passive immunity: It is observed that a young baby's immune system takes time to develop. In the uterus the fetus obtains antibodies from mother's blood, across the placenta. After birth, it will continue to receive them from mothers milk. **Colostrum,** thin yellow milk produced in the first few days after birth. This is especially rich in antibodies. These ready made antibodies help the baby to fight against pathogens. The baby has the immunity to same diseases as their mother because it has received ready made antibodies, rather than making them itself, this is said to be passive immunity as it occurs naturally so it is called **natural passive immunity.**

However passive immunity can also be provided by injections. This is not the natural way of providing immunity so it is called **artificial passive immunity.** For example if a person has cut or wound on its body, he/she needs to protect against the bacterium that cause tetanus. Tetanus is caused by the infection of bacterium *Clostridium tetani*. It is too late for a vaccination, because by the time their immune system responded, the bacterium would have multiplied and cause **fatal illness called tetanus.** Instead the person will be given an injection of antitoxin. The antitoxin will bind to the toxin produced by bacteria, rendering it harmless.

Passive immunity does not last as long as active immunity. No lymphocytes have been stimulated to produce clone of themselves, so no memory cells have been formed.

Flow Chart: 13.2



Disorders of Immune System

An autoimmune disorder is a condition arising from abnormal immune response to a normal body part. There are at least 80 types of autoimmune diseases. Nearly all body parts can be involved. Common symptoms include low grade fever, feeling tired, often symptoms appear and disappear. Some examples of autoimmune disorder are:

Allergies: Allergic diseases are number of disease conditions caused by

hypersensitivity of the immune system to some thing (Allergens) in the environment that usually causes little or no problem in most people. These diseases **cause hay fever,** food allergies, atopic dermatitis, allergic asthma etc. **Symptoms** may include red eyes, an itchy rash, sneezing, runny nose, shortness of breath or swelling.

The cause of allergies are usually genetic and environmental factors like pollen, metals, food, insect stings, drugs etc.

Usually antihistamine is given to allergic patients because in allergic conditions histamine production increases.

Transplant rejections: Transplant rejections occur when transplanted tissue is rejected by the recipient's immune system, which destroy the transplant tissue. This happens when recipients cells may recognize the donor's organ's or tissue as being foreign. As a result the recipient immune system activates against transplant organ and destroys it.

Role of T-Cells and B-Cells in transplant rejection

Rejection is an adaptive immune response via cellular immunity mediated by killer T-Cells. It induces apoptosis of T-Cells as well as humoral immunity mediated by activated B-Cells secreting antibody molecules. Although the action is joined with the components of innate immune response i.e., phagocytosis and soluble immune proteins. However different types of transplant tissues tend to favor different balances of rejection mechanisms.

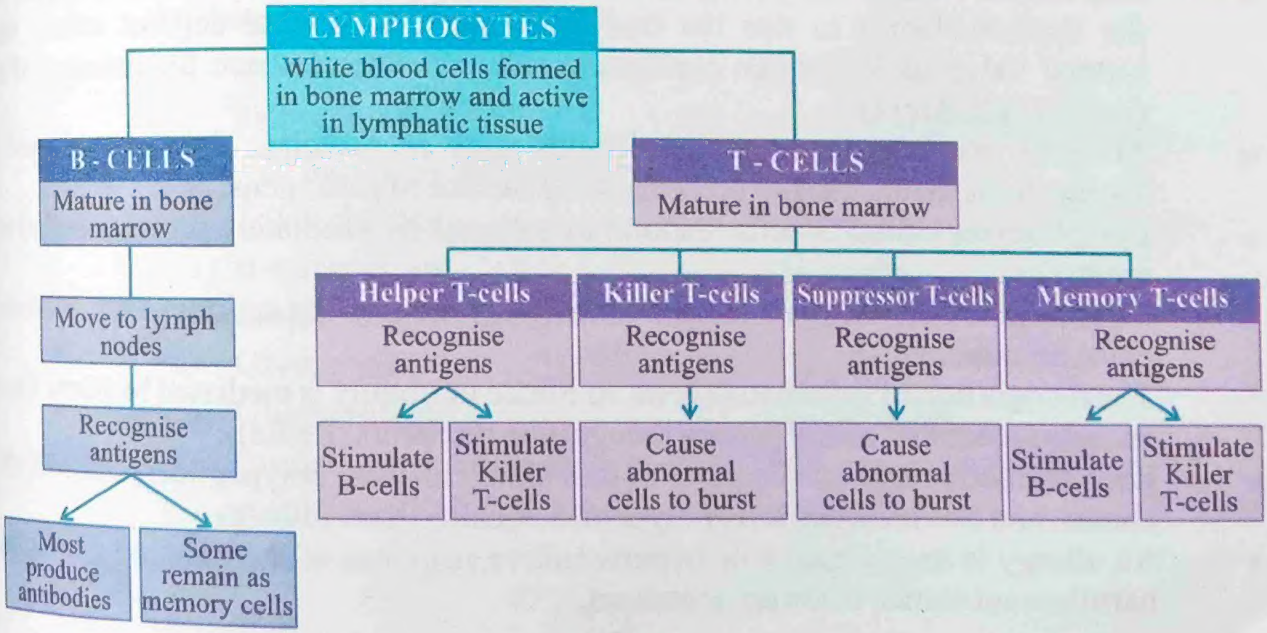
Do you know?

Stress can affect the way our immune system works. It can lead to increased level of cortisol which can blunt immune system. While positive emotions and a healthy life style may boost our immunity. Sleep deprivation can also impact.

Activity

Being too clean, can inhibit your immune system from functioning properly. Justify this statement by searching the information from different sources.

Flow chart 13.3 Different types of WBC



EXERCISE

Section I: Objective Question

Multiple choice Questions

Choose the correct answer.

A.

1. Which of the following can not induce immunity?
   (a) Bacteria (b) Parasites
   (c) Virus (d) Worms
2. Skin is a_____barrier.
   (a) Anatomical (b) Phagocytic
   (c) Physical (d) Inflammatory
3. Which among the following is anti-bacterial?
   (a) Interferon (b) hormone
   (c) Amylose (d) Protein
4. Which of the following is anti-viral?
   (a) Lysozyme (b) protein
   (c) Interferon (d) Hormone
5. Identify the phagocytic cells from the following combination.
   (a) Macrophage and Neutrophil (b) Macrophage and eosinophil
   (c) Lymphocyte and eosinophil (d) Eosinophil and neutrophil
6. Histamine is secreted by.
   (a) Epithelial cell (b) Red blood cells
   (c) Mast cells (d) White blood cells
7. Humoral immunity consists of:
   (a) Normal cells (b) Cytotoxic cells
   (c) Pathological cells (d) Immunoglobulin molecules
8. Which of the following secretes immunoglobulin.
   (a) T-lymphocyte (b) Macrophage
   (c) B-lymphocyte (d) Mast cells
9. Immunoglobulin are chemically.
   (a) Glycogens (b) Glycolipids
   (c) Glycoproteins (d) Lipoproteins
10. Colostrum is especially rich in.
    (a) Antibodies (b) Antigen
    (c) Sucrose (d) Histamine